

Synthesis, characterization and evaluation of fluorimetric chemosensors for ions based on diphenylimidazole derivatives

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Abstract: The new 2,4,5-tri-substituted imidazole derivatives **2** and **3** were obtained in good yields through a Radziszewski reaction followed by alkylation. The new derivatives were characterized by the usual spectroscopic techniques and a detailed photophysical study was undertaken. The evaluation of the compounds as fluorimetric chemosensors was carried out by performing spectrofluorimetric titrations in acetonitrile in the presence of relevant organic and inorganic anions, and of alkaline, alkaline-earth and transition metal cations.

Keywords: Chemosensors; Imidazole; Radziszewski reaction; Thiophene; Fluorescence.

1. Introduction

Chemosensors are a subject of great interest and in recent years great efforts have been made to develop fluorescent probes that are capable of detecting ions with high sensitivity and selectivity. The ideal fluorophore for chemosensory application should have high fluorescence quantum yield, high molar extinction coefficients, long-wavelengths of excitation and emission, long service life and high photostability.¹

The imidazole nucleus plays an important role in medicinal chemistry and in biochemical processes as structural component of several biomolecules and has varied pharmacological activities.² Earlier studies reported by us showed that the optical and thermal properties of imidazole derivatives could be tuned by substitution of aryl groups at positions 2, 4 and 5 by five-membered heterocycles giving rise to innovative applications of these π -conjugated systems in nonlinear optics, chemosensors and DNA intercalators.³

We now report the synthesis of new diphenylimidazoles in order to evaluate their photophysical properties and chemosensory ability. Therefore, imidazole derivative **2** bearing an heterocyclic π -bridge was obtained in good yield through a Radziszewski reaction. Direct alkylation of **2** gave the corresponding *N*-alkylated compound **3**. The new derivatives were characterized by the usual techniques and a detailed photophysical study was undertaken. The evaluation of the compounds as fluorimetric chemosensors was carried out by performing spectrofluorimetric titrations in acetonitrile in the presence of relevant organic and inorganic anions, and of alkaline, alkaline-earth and transition metal cations.

2. Experimental

2.1. Synthesis of 4,5-diphenyl-2-(5-phenylthiophen-2-yl)-1*H*-imidazole (**2**)

The heterocyclic aldehyde **1** (0.075 g, 1 mmol), diphenylethanedione (0.084 g, 1 mmol) and NH₄OAc (0.612 g, 20 mmol) were dissolved in glacial acetic acid (5 mL), followed by stirring and heating at reflux for 8 h. The mixture was then cooled to room temperature, ethyl acetate was added (15 mL) and washed with water (3 x 10 mL). After drying with anhydrous MgSO₄, the solution was filtered and the solvent was evaporated to dryness. The resulting solid was dissolved in acetone and precipitation with petroleum ether afforded the pure compound.

Compound **2** was obtained as a dark yellow solid (97 mg, 80%). Mp. 262.9-263.2 °C. UV-vis (acetonitrile): λ_{max} nm (log ϵ) 355 (4.94). ^1H NMR (DMSO- d_6 , 300 MHz): δ = 7.23 – 7.53 (m, 13H, 2x (H-2'', H-3'', H-4'', H-5'', H-6''), H-3', H-4' and H-5'), 7.55 (d, J = 4.2 Hz, 1H, H-3), 7.67 (d, J = 3.9 Hz, 1H, H-4), 7.73 (d, J = 7.75 Hz, 2H, H-2' and 6'), 12.84 (br s, 1H, NH) ppm. IR (KBr disc): ν = 3430, 3054, 2983, 2866, 2747, 1952, 1753, 1599, 1448, 1410, 1244, 1190, 1105, 1071, 919, 751, 697 cm^{-1} .

2.2. Synthesis of 1-decyl-4,5-diphenyl-2-(5-phenylthiophen-2-yl)-1H-imidazole (**3**)

Compound **2** (0.060 g, 0.16 mmol) in dry DMF (5 mL) was added dropwise under argon to a suspension of NaH (0.020 g, 4 eq.) in dry DMF (10 mL). After stirring for 0.5 h at 0°C, a solution of 1-bromodecane (0.070 g, 1.5 eq.) in dry DMF (4 mL) was added. The reaction mixture was heated for 50 h at 50 °C. The reaction was quenched with water (10 mL) and extracted with ethyl acetate (3 x 10 mL). The combined layers were dried (MgSO_4), filtered, and the solvent evaporated under reduced pressure. The resulting crude product was purified by column chromatography (silica gel, petroleum ether/diethyl ether 1:1).

Compound **3** was obtained as a yellow oil (48 mg, 58%). UV-vis (acetonitrile): λ_{max} nm (log ϵ) 265 (4.53). ^1H NMR (DMSO- d_6 , 300 MHz): δ = 0.86 – 0.89 (m, 3H, CH_3), 1.12 – 1.22 (m, 14H, 7 x CH_2), 1.60 (m, 2H, βCH_2), 4.00 (t, 2H, αCH_2), 7.22 – 7.51 (m, 13H, 2x (H-2'', H-3'', H-4'', H-5'', H-6''), H-3', H-4' and H-5'), 7.54 (d, J = 7.2 Hz, 2H, H3 and H4), 7.68 (d, J = 7.2 Hz, 2H, H2' and H6') ppm. IR (KBr disc): ν = 3425, 3061, 2926, 2854, 1729, 1664, 1601, 1481, 1445, 1369, 1264, 1073, 1028, 916, 756, 697 cm^{-1} .

2.3. Spectrophotometric and spectrofluorimetric titrations of compounds **2** and **3**

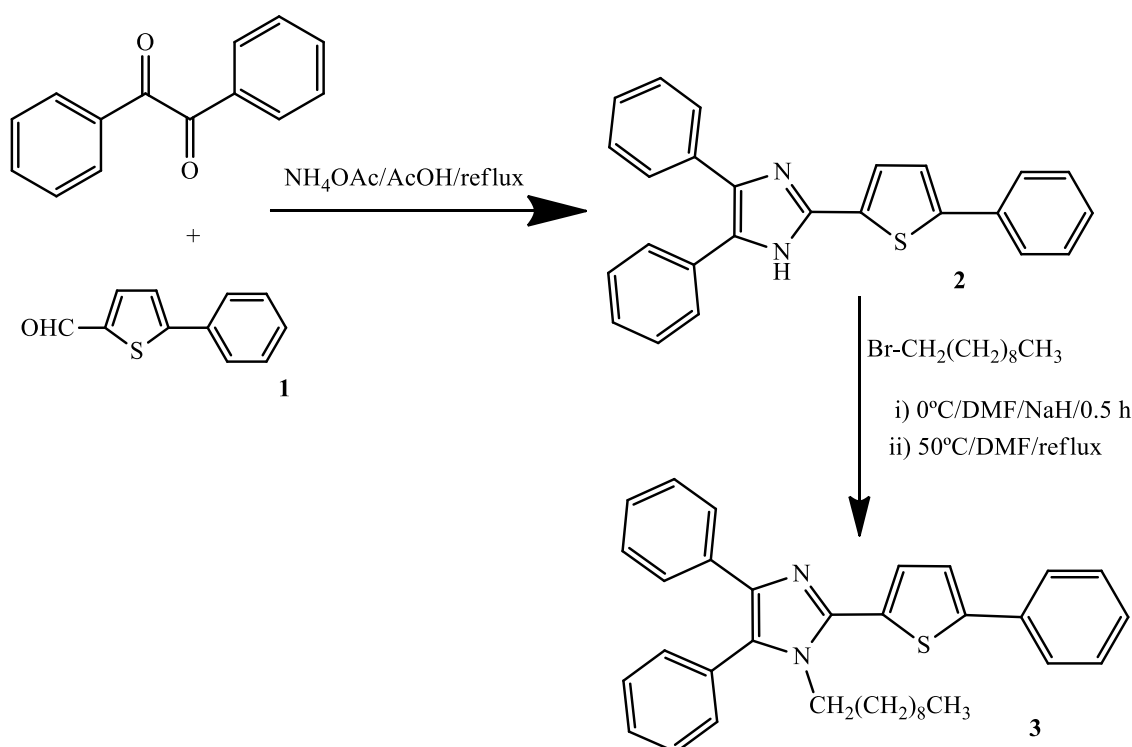
Solutions of imidazole derivatives **2** and **3** (ca. 1.0×10^{-5} M) and of the ions under study (ca. 1.0×10^{-2} to 1.0×10^{-3} M) were prepared in ACN in the presence of relevant organic and inorganic anions (AcO^- , F^- , Cl^- , Br^- , CN^- , NO_3^- , BzO^- , H_2PO_4^- , HSO_4^-), and of alkaline, alkaline-earth and transition metal cations (Cu^{2+} , Cd^{2+} , Pd^{2+} , Ni^{2+} , Hg^{2+} , Zn^{2+} , Fe^{2+} , Fe^{3+} and Cr^{3+}).

Titration of compounds **2-3** was performed by the sequential addition of ion to the diphenylimidazole derivatives solution, in a 10 mm path length quartz cuvette and emission spectra were measured by excitation at the wavelength of maximum absorption for each compound, indicated in Table 1.

3. Results and discussion

3.1. Synthesis and characterization

The new imidazoles **2** and **3** bearing an arylthiophene bridge, were synthesized in moderate to good yields (58-80 %), by Radziszewski reaction between aldehyde **1** and benzil followed by alkylation (Scheme). The new compounds were completely characterized by the usual spectroscopic techniques (Table 1).



Scheme. Synthesis of 2,4,5-tri-substituted imidazole derivatives **2** and **3**.

Table 1. Yields, UV-visible absorption and fluorescence data for imidazoles **2** and **3** in acetonitrile solution.

Imidazole	Yield (%)	UV/Vis			Fluorescence	
		λ_{max} (nm)	$\log \epsilon$	λ_{em} (nm)	Φ_{F}	Stokes' shift (nm)
2	80	355	4.94	443	0.44	88
3	58	265	4.53	435	0.42	170

The absorption and emission spectra of imidazoles **2** and **3** were measured in acetonitrile solutions (Table 1). Imidazole derivatives **2** and **3** have the same

heterocyclic π -bridge, and differ only in the substituent on the nitrogen of the imidazole ring.

The relative fluorescence quantum yields were determined by using 10^{-6} M solutions of DPA in ethanol as standard ($\Phi_F = 0.95$).⁴ For the Φ_F determination, the fluorescence standard was excited at the wavelengths of maximum absorption found for each of the compounds to be tested and in all fluorimetric measurements the absorbance of the solution did not exceed 0.1. Diphenyl-imidazoles **2** and **3** exhibited excellent fluorescence quantum yields in acetonitrile ($\Phi_F = 0.42$ and 0.44) (Table 1).

3.2 Spectrophotometric/spectrofluorimetric titrations and chemosensing studies of **2** and **3** with metallic ions

Compounds **2** and **3** (10^{-5} M) were evaluated as chemosensors in the presence of several relevant ions (AcO^- , F^- , Cl^- , Br^- , CN^- , NO_3^- , BzO^- , H_2PO_4^- , HSO_4^- , Cu^{2+} , Cd^{2+} , Pd^{2+} , Ni^{2+} , Hg^{2+} , Zn^{2+} , Fe^{2+} , Fe^{3+} and Cr^{3+}). Spectrophotometric and spectrofluorimetric titrations were carried out in ACN solutions, in order to evaluate their chemosensory ability.

Spectrofluorimetric titrations of compound **2** revealed its ability to act as fluorimetric chemosensor for certain anions and cations. On the other hand, for compound **3**, the introduction of an alkyl chain in the NH group of the imidazole heterocycle lead to a selective fluorimetric chemosensor for Fe^{3+} and Hg^{2+} (Table 2). For the remaining ions, no changes in the fluorescence intensity were seen upon titration. As a preliminary test, the differences in fluorescence intensity of compound **2** alone and in the presence of 100 equivalents of several ions in acetonitrile solution can be seen in Figure 1.

Spectrophotometric titrations did not reveal interaction with any of the cations and anions tested.

Table 2. Results obtained in spectrofluorimetric titrations in acetonitrile in the presence of several ion solutions for imidazoles **2** and **3**.

Imidazole	Anion/Cation					
	F^-	CN^-	AcO^-	Fe^{3+}	Cu^{2+}	Hg^{2+}
2	✓	✓	✓	✓	✓	
3				✓		✓

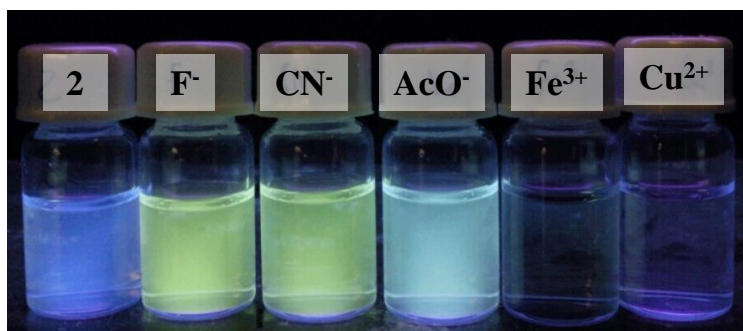


Figure 1: Acetonitrile solutions of compound **2** and compound **2** in the presence of 100 equivalents of several ions, visualized in a UV chamber under a 365 nm lamp.

In the spectrofluorimetric titrations with Fe^{3+} , a strong decrease of the fluorescence intensity (a chelation enhancement of quenching, CHEQ effect) was observed for the two derivatives, with a complete fluorescence quenching (**2**, 165 eq.; **3**, 171 eq.) (Figure 2). A total quenching in the fluorescence was also achieved for compound **3** in the presence of Hg^{2+} .

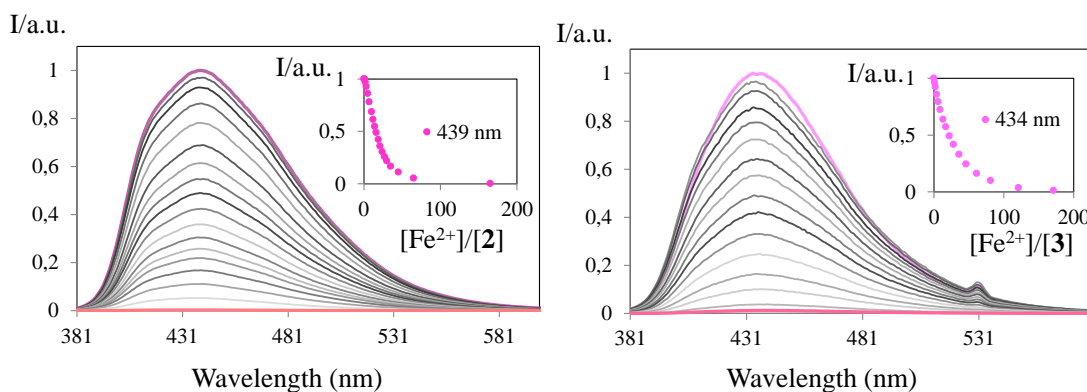


Figure 2: Spectrofluorimetric titrations of compounds **2** and **3** with addition of increasing amounts of Fe^{3+} in ACN. The inset represents the normalized emission ($[\mathbf{2}] = [\mathbf{3}] = 1 \times 10^{-5} \text{ M}$, $T = 298 \text{ K}$).

Spectrofluorimetric titrations of derivative **2** with F^- , CN^- , AcO^- and Cu^{2+} , showed a strong decrease of the fluorescence intensity with an almost complete fluorescence quenching. Two representative examples of spectrofluorimetric titrations of **2** with CN^- and F^- are shown in Figure 3.

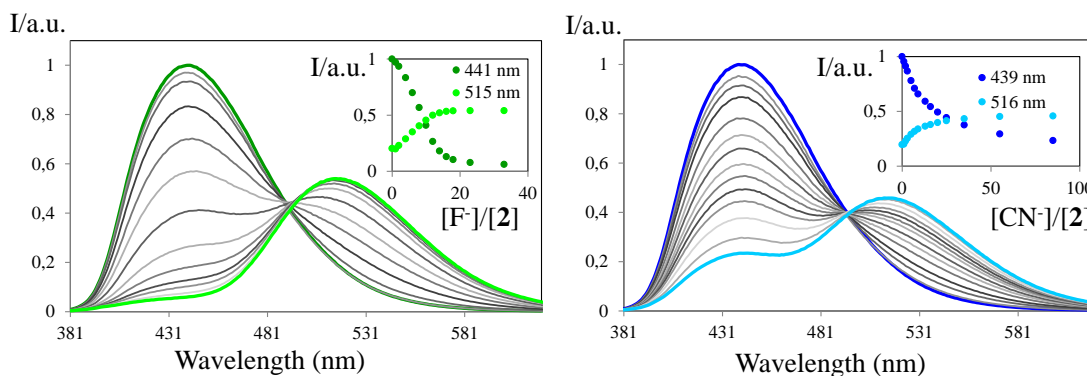


Figure 3: Spectrofluorimetric titrations of compound **2** with addition of increasing amounts of F^- and CN^- in ACN. The inset represents the normalized emission ($[2] = 1 \times 10^{-5} \text{ M}$, $T = 298 \text{ K}$).

Spectrofluorimetric titrations of compound **2** in presence of CN^- and F^- ions revealed that the plateau was achieved after the addition of 33 equivalents of F^- ion whereas 85 equivalents of CN^- ion were needed. In both titrations, the intensity of the emission band was reduced (CHEQ effect), accompanied by a red-shift, and a new band was formed, with an iso-emissive point at 513 nm with CN^- ion and 518 nm with F^- ion, indicating the presence of two emissive species in the solution.

4. Conclusions

The synthesis of new imidazole derivatives **2** and **3** was achieved in moderate to good yields by simple experimental procedures. The photophysical properties were evaluated by fluorescence spectroscopy and revealed that the imidazole derivatives are highly emissive.

The sensory ability was evaluated for several ions by spectrofluorimetric titrations in acetonitrile. Compound **2** show higher sensitivity for F^- , CN^- , AcO^- and also for Fe^{3+} and Cu^{2+} , compared to the other ions tested. On the other hand, compound **3** exhibit sensitivity and selectivity only for Hg^{2+} and Fe^{3+} . Therefore modulation of the chemosensor ability for imidazole derivatives **2-3** was achieved by alkylation of the free NH group of the imidazole heterocycle.

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